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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/049,427
Filing Date: May 6, 2002
Appellant(s): KARL THOR

Gary J. Connell
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/1/2007 appealing from the Office action mailed 10/3/2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of the claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

McMahon et al. (*J. Urology*, 161, 1826-30)

Lane (*J. Psychopharmacology*, 11(1), 72-82)

Eli Lily (ZA 9300694)

Robertson et al. (US Patent 5,135,947)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-42 and 51-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over McMahon et al. (*J. Urology*, 161, 1826-30) and Lane (*J. Psychopharmacology*, 11(1), 72-82) in view of Eli Lily (ZA 9300694) and Robertson et al. (US Patent 5,135,947).

McMahon et al. teaches the treatment of premature ejaculation with oral doses of paroxetine hydrochloride (an SSRI) as needed (Title). The treatment is taught as being administered on an as needed basis without a priming dose 3-4

hours prior to planned intercourse (Abstract). SSRIs are taught in general to delay orgasm and reduce sexual excitement thereby having a beneficial effect on premature ejaculation (2nd and 3rd paragraphs of p. 1826).

Lane teaches SSRIs for the management of premature ejaculation (Abstract; p. 79). Lane also teaches low dosages of SSRIs administered on an as needed basis prior to intercourse for the treatment of premature ejaculation (p. 79, 2nd col., 1st full paragraph).

Eli Lilly teaches the treatment of premature ejaculation with the SSRIs fluoxetine, dapoxetine, and duloxetine (pp. 1 and 5).

Robertson et al. teaches sluoxetine, serotonin and the compounds as instantly claimed as known in the art as SSRIs (col. 1, lines 15-66; col. 3, lines 35-36; col. 23, lines 1-24 and 48-60; col. 24, lines 46-58). Oral administration of the compounds are taught (col. 19, lines 22-24).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the specific compounds of McMahon et al. and Lane with the compounds as instantly claimed because (1) McMahon et al. teaches the treatment of premature ejaculation with various SSRIs; (2) McMahon et al. teaches that SSRIs cause delayed orgasm and reduced sexual excitement thereby having a beneficial effect on premature ejaculation; (3) Lane teaches that SSRIs may be used in the management of premature ejaculation; (4) Eli Lilly teaches the treatment of premature ejaculation with the compounds as instantly claimed; and (5) Roberson et al. teaches the instantly claimed compounds as SSRIs. Accordingly, absent a showing of unexpected results, it would have been

obvious to one of ordinary skill in the art to utilize the known SSRIs of Robertson et al. in the treatment of either McMahon et al. or Lane. One would have been motivated to substitute the SSRIs of McMahon et al. and Lane with the SSRIs as instantly claimed because of an expectation of success in treating premature ejaculation with an SSRI, as taught by both McMahon et al. and Lane.

It would have been obvious to one of ordinary skill in the art to administer the instantly claimed compounds in the dosages claimed and at the times claimed because "[w]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

(10) Response to Argument

Appellant argues in the Declaration of David A. Rivas that McMahon et al. conclusions regarding as needed dosing of paroxetine does not allow the skilled artisan to draw any conclusions about whether or not as needed use of paroxetine in the absence of priming doses is efficacious because the "as needed" use of paroxetine in McMahon et al. does not preclude priming doses. Rivas states, "without prior 2 week daily dosing" in Study 1 is not "in the absence of a priming dose." Rivas also states that the "as needed" use of paroxetine in Study 1 was not designed to avoid a priming dose effect.

The Declaration under 37 CFR 1.132 filed 7/28/2006 is insufficient to overcome the rejection of claims 37-42, 51-54 based upon McMahon et al. as set forth in the last Office action because: the interpretation of the reference by Rivas

is incorrect. Nowhere in the reference, especially in Study 1, does it state the need to administer a priming dose or refer to a priming dose effect. In essence, the absence of such statements has prompted the incorrect conclusions concerning the requirement of any priming doses.

Rivas argue that McMahon et al. study design did not impose a minimum time interval between intercourse episodes and therefore, paroxetine from one dose that was not cleared from the body could, in combination with a subsequent dose, result in paroxetine exposure in the patient greater than a single dose, thereby functioning as a priming dose. This is not persuasive because although McMahon et al. states "paroxetine as needed is significantly better if patients are initially treated with the drug daily," there is no doubt that paroxetine still increases mean ejaculatory latency time without daily dosing.

Rivas argue that McMahon et al. does not provide sufficient information to determine whether the week 1 treatment data of Study 1 are statistically significantly different from the control data. Again, an incorrect conclusion is made because although McMahon et al. states statistically superior results for weeks 2-4, this does not preclude any positive results for week 1. *In fact, as reported in Table 2, an increase in ejaculatory latency time was observed in week 1 when compared to the placebo. McMahon et al. also clearly shows increased ejaculatory latency times in week 1 compared to a placebo (increase to 1.0 min from 0.3 min) as shown in Figure 1. Furthermore, in the discussion section, McMahon corroborates this statement by stating that within 1 to 2 weeks of paroxetine administration, ejaculatory times were prolonged.*

Appellant argues, "by [McMahon et al.'s] admission, [] there was no statistically superior increase in ejaculatory latency in the first week." This argument is not persuasive. First, the argument presupposes that the dosing during the first week of administration is, effectively, equivalent to a "priming dose". If such an argument were found to be persuasive, however, it would suggest that for a drug to be administered on an "as needed" basis in the absence of a priming dose, only the first administration of the drug would qualify as "as needed" in the absence of a priming dose. Second, the language of the disclosure clearly suggests that while a priming dose is preferred, it is not required. McMahon states that "paroxetine as needed was significantly better if patients were initially treated with the drug daily." Such a suggestion would indicate to one of ordinary skill in the art that the effects of administration are the best when there is a priming dose, but that the administration of the drug in the absence of a priming dose would also be effective at achieving the desired results. Accordingly, Appellant's suggestion that Examiner is required to provide evidence that the data is of McMahon et al. for the first week is statistically significant when McMahon et al. says that it is not is not necessary. Furthermore, McMahon et al. clearly illustrates (Figure 1) that the mean ejaculatory interval was seen to increase after one week of administration of paroxetine in both Groups A and B by identical amounts and that the increase was more than that observed for placebo. The multiple of increase seen in Groups A and B (weeks 1 and 8, respectively) are comparable to those set forth in the instant specification (see, e.g., Table 9). Furthermore, it is noted that

McMahon et al. does not state that the results of week 1 are *not* statistically superior. Accordingly, one of skill in the art would look to Fig. 1 to determine the results of week 1, wherein the skilled artisan would observe the increases in mean ejaculatory interval, as discussed above.

Appellant argues that in McMahon et al., "neither the design or the results of the studies would lead one of skill in the art to conclude that an SSRI could be used to treat PE patients on an as-needed basis." This argument is not persuasive because McMahon et al. clearly teaches the administration of the SSRIs therein on an "as needed" basis. See Abstract; p. 1827, Study 1; etc. When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980).

Appellant attempt to rebut the presumption of operability of McMahon et al. by arguing that "[t]he McMahon study did not use an appropriate number of men suffering with PE to address the study objective" and that "[t]he McMahon studies were single-blind studies". These arguments are not persuasive because Appellant's allegation that there are an insufficient number of test subjects does not address the presumption of operability, but the "scientific validity". There is no reasons to assume that the standard required for one of ordinary skill in the art to accept the teachings of McMahon et al. as scientific certainty would be the same as the standard required for one of ordinary skill in the art to *presume* that

the invention would *work*. It is further noted that there is no supporting documentation that McMahon's number of test subjects is insufficient for "scientific validity". Appellant's arguments regarding the single-blind studies are, likewise, unpersuasive. Appellant's argument that "on average, trials that have not used appropriate levels of blinding, such as McMahon, show larger treatment effects than blinded studies" is not sufficient to suggest to the skilled artisan that the teachings of McMahon should not be presumed enabled. First, it is noted that the teaching merely suggests that "on average" different levels of blinding produce different results. Second, there is only a suggestion that varying levels of blinding may lead to varying magnitudes of efficacy, not that the efficacy is, itself, questioned.

Appellant argues that because Lane states that "[t]he placebo-controlled studies with sertraline and paroxetine used high doses. The efficacy of the lower doses and different dosing regimens has yet to be fully explored" that Lane "questions the applicability of these two initial reports to the clinical use of sertraline and paroxetine themselves and certainly does not support the general efficacy of SSRIs in the treatment of PE." This argument is not persuasive because Lane does not suggest that the treatment does not work but merely that, as with all drugs, dosage optimization must be determine and that once such a dosage optimization is determined that a cost/benefit analysis of the side effects and treatment benefits must be weighed.

Appellant argues that Lane's review of Swartz's "seemingly amazing results, that are inconsistent with any results available at that time, or that have

been published subsequent to that report appear to have been an average of both daily and as-needed dosing." This argument is not persuasive because even if the results were indeed an average of both daily and as-needed dosing, such an averaging would not take away from the fact that Swartz via Lane clearly teaches administration on an as needed basis.

Appellant argues that the Swartz teaching that "the '26-hour elimination half life [of sertraline] allows considerable liberties in dosing schedules" indicates that the teaching is a "preliminary case report and, even in combination with the high dose studies of paroxetine and sertraline, one of skill in the art clearly would not regard this report as supporting that all SSRIs, administered in low doses on an as-needed basis prior to intercourse would be efficacious in treating PE." This argument is not persuasive because the teaching that there are considerable liberties in dosing schedules indicates merely that there are considerable liberties in dosing schedules or, in other words, that administration schedules may be adjusted to the particular needs of a patient. Furthermore, the Abstract of Lane clearly teaches, "selective serotonin reuptake inhibitors (SSRIs) are clearly associated with delayed ejaculation ...". This teaching, coupled with the other references, particularly Eli Lilly and Robertson et al., that it would have been obvious to treat PE with dapoxetine. Furthermore, administration of SSRIs on an as-needed basis is disclosed as being efficacious by both Lane and McMahon et al., as discussed above.

Examiner respectfully reminds Appellant that the standard for obviousness is not absolute but a reasonable expectation of success.

Appellant argues that the obviousness rejection is based on impermissible "obvious to try" standard as it applies to substituting dapoxetine for the compounds of McMahon or Lane to arrive at the claimed method of treating PE.

This is not persuasive in view of the Supreme Court Decision in KSR International Co. v. Teleflex Inc. where new rationales were set to arrive at a conclusion of obviousness. These include simple substitution of one known element for another to obtain predictable results and applying an "obvious to try" rationale where one is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. Applying this rationale to the cited prior art, the rejection is based on substituting the SSRIs as disclosed by McMahon and Lane with another SSRI, specifically dapoxetine, as disclosed by Eli Lilly. Lane teaches the use of SSRIs broadly. Eli Lilly and Robertson disclose finite embodiments of SSRIs as known in the art. Furthermore, Appellant has admitted on record that SSRI's are known to affect sexual function and have been suggested for treatment of PE (Appeal Brief, pg. 9, last paragraph). Therefore, a predictable potential solution to a recognized problem or need in the art had been identified by the Appellant. Moreover, as one of ordinary skill in the art is simply substituting one SSRI with another, a reasonable expectation of success in treating PE with an SSRI has been made in view of the cited prior art teachings.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

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SUPERVISORY PATENT EXAMINER

Respectfully submitted,

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August 2, 2007

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